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Optimization of the cyclotron radioisotopes production and purification process using an automated solid targets irradiation system

The automated process for the production and purification of copper and zirconium radioisotopes produced by irradiating solid targets in the variable energy (14-19 MeV) cyclotron (TR19, ACSI Canada) has been optimized, using a commercially available automated solid target system comprising modules for electrodeposition, pneumatic transfer, irradiation, dissolving and purification (Alceo 2.0, Comecer, Italy). The default process-script was modified as result of the local set-up and particularities.

In addition to a convenient half-life of 12.7 hours, copper-64 has several attributes, such as a complex decay scheme, comprising electron capture (43%), beta emission (39%), and positron emission branches (18%), adding to its biochemical implications in oncogenesis a huge potential to exploit nuclear medicine applications.

In the recent years, PET imaging with ^{89}Zr -based agents has been a dynamic field of research, its disintegration taking place through increased electron uptake (76.6%) and positron emission (22.3%). ^{89}Zr has a relatively long half-life of about 3.3 days, making it ideal for use in nuclear imaging studies when pairing with slow pharmacokinetic carriers such as full antibodies. It also proved to be very useful in therapy follow-up imaging, using highly specific biovectors.

Copper-64: The process involves enriched ^{64}Ni electrodeposition on a platinum support attached to a transfer shuttle. Parameters such as proton beam current intensity and energy, target positioning/geometry and irradiation time were adapted to optimize the production yield of the final product. The target was irradiated via $^{64}\text{Ni}(p,n)^{64}\text{Cu}$ reaction, dissolved in an automatic module (Taddeo Synthesis Module, Comecer) by using 6M hydrochloric acid and negative voltage at 90°C . The resulted solution is automatically switched to the purification module, where an ion exchange resin (AG1X8) was used and eluted with HCl solutions of different concentrations. The irradiation process yielded to an activity of 15.42 ± 1.57 GBq EOB, beam intensity set at $25\mu\text{A}$, beam energy degraded to 11.7 MeV and 6 hrs irradiation time. The radiochemical purity, assessed by radio-TLC and radio-HPLC, was higher than 99% after purification.

Zirconium-89: The production on natural yttrium foils targets, via $^{89}\text{Y}(p,n)^{89}\text{Zr}$ reaction was optimized by modifying the input parameters, such as current intensity, and energy of the proton beam on target, and the irradiation time. After irradiation, the target was dissolved and the process was performed manually, using hydrochloric acid at 80°C . The resulted solution was purified on a Zr cartridge (Triskem). The irradiation process yielded an activity of 2.7 ± 0.25 GBq EOB, with a beam current of $25\mu\text{A}$, energy degraded at 11.9 MeV on target, and an irradiation time of 4 hrs. The radiochemical purity, assessed by radio-TLC, was 98% after purification, optimized by using a different concentration of oxalic acid for elution from purification cartridge, getting a radiochemical solution suitable for radiolabelling use.

The automated solid targets irradiation system can be also used for cyclotron production of other metallic radioisotopes of interest for PET imaging and/or targeted therapy, yielding to high purity and radioactivity concentration solution of pharmaceutical grade.

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